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31. A method according to claim 7, wherein said first bioactive agent is said first identifier binding ligand. - -

REMARKS

Claims 1-7 and 15 -31 are pending. For the Examiners convenience a copy of the currently pending claims is appended hereto. Support for the amendment to Claims 1, 2, 6 and 7 is found at p. 8, lines 16 and 27. In addition, the claims are amended for clarity. Support for the amendment of claims 3-5 and 15 is found in the claims as filed. Support for claim 17 is found in claim 2 as filed and p. 9, line 20. . Support for claims 18-21 is found at p. 9, lines 10-17. Support for claims 22 and 23 is found in claims 1 and 2, respectively, as filed, at p. p. 26, line 31, and p. 27, lines 1-3. Support for claims 24 and 25 is found in claims 6 and 7, respectively, as filed, at p. 26, line 31 and p. 27, lines 1-3. Support for new claims 26 and 27 is found at p. 26, line 31 and p. 27, lines 1-3. Support for new claims 28 and 29 is found at p. 27, lines 10-19. Support for new claims 30 and 31 is found at p. 7, lines 25-29, and at p. 12, lines 26-30.

RESPONSE TO REJECTIONS

Rejection Under 35 U.S.C. § 112.

Currently pending claims 1-7 and 15-16 are rejected under 35 U.S.C. § 112, first paragraph for lack of written description. Basically the Office Action suggests that the "limitation of discrete or individual sites on the substrate for microsphere attachment is separate from random distribution of microspheres." The Examiner points to p. 9, line 30 to p. 10, line 17 as support for the assertion that "patterning of sites ... is an alternative to a random distribution and not practiced at the same time." Applicants respectfully traverse.

Although Applicants agree that p. 9, line 30 to p. 10 line 17 indicates that the substrate may contain patterned sites or alternatively it may contain random distribution of sites, this section in no way describes that manner in which microspheres are distributed on the surface. That is, the specification is describing that the sites on the surface of the substrate may be

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arranged in a pattern or may be random. As noted by the Examiner, at p. 10, line 7, the "sites may be a pattern...or randomly distributed."

However, as noted in the previous Response to Office Action, the specification is replete with disclosure related to the random distribution of microspheres on a patterned substrate. As indicated at p. 6, lines 30-31, "[t]he beads may be randomly distributed on the array". At p. 6, lines 19-20 is noted that "beads, also termed microspheres, ...are distributed on a substrate comprising a patterned surface of discrete sites". At p. 6, lines 26-27 is noted that "the beads are randomly distributed on a patterned surface."

Accordingly, in contrast the Examiner's assertion that inclusion of the term "random" in the claims constitutes new matter, Applicants submit that the specification fully supports the claims as currently pending. As noted above, the specification clearly describes that microspheres may be randomly distributed on a patterned surface. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

Rejections Under 35 U.S.C. § 102(b) and (e)

Currently pending claims 1-7 and 15-16 stand rejected under 35 U.S.C. § 102(b) and (e) as being anticipated by Ekins et al. (U.S.P.N. 5,516,635). It is acknowledged that the Examiner has maintained and reiterated the rejection from the previous office action; the rejection is maintained in part "due to anticipation of removal of the ... NEW MATTER". Applicants respectfully traverse the rejection.

Initially, Applicants assert for the reasons described above, that the claims as pending contain no new matter. That is, the specification fully supports claims directed to microspheres randomly distributed on a surface. Accordingly, the claims have not been amended to remove this language.

As such, Applicants submit that Ekins fails to teach random distribution of microspheres on a surface comprising discrete sites. In fact, Ekins teaches the opposite, that microspheres are targeted to particular locations by an antibody attached to the bead. That is, the capture binding

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agent, which is spotted on the substrate, defines the site to which the beads attach. Accordingly, Applicants submit that Ekins fails to anticipate any of the present claims.

Moreover, Applicants submit that Ekins fails to teach a substrate with a surface comprising discrete sites at a density of at least 100 sites per 1mm^2 . That is, while Applicants note that Ekins provides that the capture binding agent "is deposited on a solid support in the form of one or more microspots having an area of 1mm^2 down to $100\text{ }\mu\text{m}^2$, or less," this density is still an order of magnitude less than the density recited in claims 1, 2, 6 or 7. As such, Applicants submit that Ekins fails to teach each element of claims 1, 2, 6 or 7 and those that depend from these claims.

In addition, as to the Examiner's rejection of claim 2 and 6, Applicants respectfully note that Ekins fails to teach that microspheres do not have labels. Indeed, the point of Ekins is to provide microspheres that have labels to detect binding reactions. Accordingly, Applicants submit that Ekins fails to anticipate claims 2 and 6 and those claims that depend from these claims.

Finally, Applicants draw the Examiner's attention to the newly submitted claims. Applicants note that new claim 17 recites that the substrate is a fiber optic bundle. Applicants submit that there is no teaching of fiber optic bundles in Ekins. New claim 22 is drawn to a composition that includes first and second decoder binding ligands bound to first and second identifier binding ligands. Likewise, new claim 25 is drawn to a method of making a composition that includes the step of binding a first and second decoder binding ligand to a first and second identifier binding ligand. Applicants submit that there is no teaching in Ekins of such a composition or method. That is, Ekins fails to teach decoder binding ligands bound to identifier binding ligands.

New claim 23 is drawn to a composition including first and second decoder binding ligands bound to first and second bioactive agents, wherein the microspheres do not comprise a label. Likewise, new claim 24 is directed to a method of making a composition including binding a first and second decoder binding ligand to first and second bioactive agents, wherein

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the microspheres to do not comprise a label. Applicants submit that there is no teaching in Ekins of such a composition or method. That is, Ekins fails to teach decoder binding ligands bound to bioactive agents. In addition, as described above, Ekins fails to teach arrays wherein the microspheres do not comprise a label.

Accordingly, Applicants submit that Ekins fails to anticipate any of the presently pending claims. Applicants respectfully request withdrawal of the rejections.

CONCLUSION

Applicants submit that the claims as amended are in form for immediate allowance and the Examiner is respectfully requested to early notification to that effect. The Examiner is invited to contact the undersigned at (415) 781-1989 if any issues may be resolved in that manner.

Respectfully submitted,

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APPENDIX- CURRENTLY PENDING CLAIMS

1. (Amended) An array composition comprising:

- a) a substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm²; and
 - b) a population of microspheres comprising at least a first and a second subpopulation, wherein [each] said first and said second subpopulations comprise[s]:
 - i) a first and second bioactive agent, respectively; and
 - ii) a[n] first and second identifier binding ligand, respectively [that will bind a decoder binding ligand, such that the identification of the bioactive agent can be elucidated];
- wherein said microspheres are randomly distributed on said surface.

2. (Amended) An array composition comprising:

- a) a substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm²; and
- b) a population of microspheres comprising at least a first and a second subpopulation, wherein [each] said first and second subpopulations comprise[s] a first and second bioactive agent, respectively, and [does] do not comprise [an optical signature] a label, wherein said microspheres are randomly distributed on said surface.

3. (Amended) A composition according to claim 1 [or 2], 2 or 17, further comprising at least one decoder binding ligand.

4. (Amended) A composition according to claim 1 [or 2], 2, 17, 22 or 23, wherein said bioactive agents are nucleic acids.

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5. (Amended) A composition according to claim 1 [or 2], 2, 17, 22 or 23, wherein said bioactive agents are proteins.

6. A method of making a composition comprising:

a) [forming] providing a surface comprising individual sites on a substrate at a density of at least 100 sites per 1 mm²;

b) randomly distributing microspheres on said surface such that said individual sites contain microspheres, wherein said microspheres comprise at least a first and a second subpopulation, [each] wherein said first and second subpopulations [comprising] comprise a first and a second bioactive agent, respectively, and do not comprise [an optical signature] a label.

7. A method of making a composition comprising:

a) [forming] providing a surface comprising individual sites on a substrate at a density of at least 100 sites per 1 mm²;

b) randomly distributing microspheres on said surface such that said individual sites contain microspheres, wherein said microspheres comprise at least a first and a second subpopulation[s], wherein said first and second subpopulations [each comprising] comprise:

i) a first and second bioactive agent, respectively; and

ii) [an] a first and a second identifier binding ligand [that will bind at least one decoder binding ligand, such that the identification of the bioactive agent can be elucidated].

15. (Amended) The composition according to claim 1 [or claim 2] 2, 17, 22 or 23, wherein said discrete sites are wells.

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16. (Amended) The method according to claim 6[, claim], 7, 24 or 25, [claim 8, claim 13 or claim 14,] wherein said discrete sites are wells.

Please add the following new claims:

--17. An array composition comprising:

- a) a substrate with a surface comprising discrete sites, wherein said substrate is a fiber optic bundle; and
- b) a population of microspheres comprising at least a first and a second subpopulation, wherein each subpopulation comprises a bioactive agent and does not comprise a label, wherein said microspheres are randomly distributed on said surface.

18. A composition according to claim 1, 2, 22 or 23, wherein said substrate is selected from the group consisting of glass and plastic.

19. A composition according to claim 1, 2, 22 or 23, wherein said substrate is a fiber optic bundle.

20. A method according to claim 6, 7, 24 or 25, wherein said substrate is selected from the group consisting of glass or plastic.

21. A method according to claim 6, 7, 24 or 25 wherein said substrate is a fiber optic bundle.

22. An array composition comprising:

- a) a substrate with a surface comprising discrete sites; and
- b) a population of microspheres comprising at least a first and a second subpopulation, wherein said first and second subpopulations comprise:
 - i) a first and a second bioactive agent, respectively;

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ii) a first and second identifier binding ligand, respectively; and
iii) a first and a second decoder binding ligand, bound to said first and second identifier binding ligands, respectively;
wherein said microspheres are randomly distributed on said surface.

23. An array composition comprising:

- a) a substrate with a surface comprising discrete sites; and
 - b) a population of microspheres comprising:
 - i) at least a first and a second subpopulation, wherein said first and second subpopulations comprise a first and a second bioactive agent, respectively, and do not comprise a label; and
 - ii) a first and a second decoder binding ligand bound to said first and second bioactive agent, respectively;
- wherein said microspheres are randomly distributed on said surface.

24. A method of making a composition comprising:

- a) providing a surface comprising individual sites on a substrate;
 - b) randomly distributing microspheres on said surface such that said individual sites contain microspheres, wherein said microspheres comprise at least a first and a second subpopulation comprising a first and second bioactive agent, respectively; and
 - c) binding a first and second decoder binding ligand to said first and second bioactive agent, respectively;
- wherein said microspheres do not comprise a label.

25. A method of making a composition comprising:

- a) forming a surface comprising individual sites on a substrate;
- b) randomly distributing microspheres on said surface such that said individual sites

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contain microspheres, wherein said microspheres comprise at least a first and a second subpopulations, wherein said first and second subpopulations comprise:

- i) a first and second bioactive agent, respectively; and
- ii) a first and second identifier binding ligand, respectively,
- c) binding a first and second decoder binding ligand to said first and second identifier binding ligand.

26. A method according to claim 6 further comprising:

- c) binding a first and second decoder binding ligand to said first and second bioactive agent.

27. A method according to claim 7 further comprising:

- c) binding a first and second decoder binding ligand to said first and second identifier binding ligand.

28. A method according to claim 24, 25, 26 or 27, wherein at least said first decoder binding ligand comprises a label.

29. A composition according to claim 3, wherein said at least one decoder binding ligand comprises a label.

30. A composition according to claim 1, wherein said first bioactive agent is said first identifier binding ligand.

31. A method according to claim 7, wherein said first bioactive agent is said first identifier binding ligand. - -